

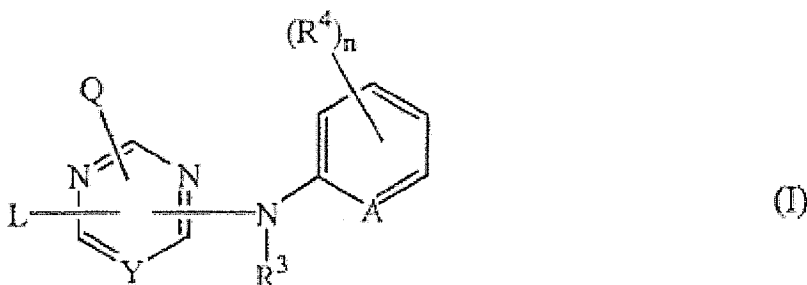
AMENDMENTSAmendments to the Claims

Please amend the claims according to the following listing of the claims.

Listing of the claims

1. (currently amended) Rate-controlled release particles, comprising, in a polymer matrix consisting of from 40 to 70% by weight of the total weight of the rate-controlled release particles of a homo- or copolymer of N-vinylpyrrolidone, an active ingredient as a solid dispersion in the polymeric matrix and from 5 to 25% ~~b.w.~~ by weight of the total weight of the rate-controlled release particles of hydroxypropyl methyl cellulose, and optionally further comprising a surfactant, wherein the rate-controlled release particles are obtained by forming a homogeneous mixture of the components in the form of a melt, extruding said mixture and shaping of the extrudate, and wherein the active ingredient is

a compound of formula I



a N-oxide, a pharmaceutically acceptable addition salt or a stereochemically isomeric form thereof, wherein

Y is CR⁵ or N;

A is CH, CR⁴ or N;

n is 0, 1, 2, 3 or 4;

Q is -NR¹R² or when Y is CR⁵ then Q may also be hydrogen;

R¹ and R² are each independently selected from hydrogen, hydroxy, C₁₋₁₂alkyl, C₁₋₁₂alkyloxy, C₁₋₁₂alkylcarbonyl, C₁₋₁₂alkyloxy carbonyl, aryl, amino, mono- or di(C₁₋₁₂alkyl)amino, mono- or di(C₁₋₁₂alkyl)aminocarbonyl

wherein each of the aforementioned C₁₋₁₂alkyl groups may optionally and each individually be substituted with one or two substituents each independently selected from hydroxy, C₁₋₆alkyloxy, hydroxy-C₁₋₆alkyloxy, carboxyl, C₁₋₆alkyloxy carbonyl, cyano, amino, imido, aminocarbonyl, aminocarbonylamino, mono- or di(C₁₋₆alkyl)amino, aryl and Het; or

R¹ and R² taken together may form pyrrolidinyl, piperidinyl, morpholinyl, azido or mono- or di(C₁₋₁₂alkyl)aminoC₁₋₄-alkylidene;

R³ is hydrogen, aryl, C₁₋₆alkylcarbonyl, C₁₋₆alkyl, C₁₋₆alkyloxy carbonyl, C₁₋₆alkyl substituted with C₁₋₆alkyloxy carbonyl; and

each R⁴ independently is hydroxy, halo, C₁₋₆alkyl, C₁₋₆alkyloxy, cyano, aminocarbonyl, nitro, amino, trihalomethyl, trihalomethyloxy, or when Y is CR⁵ then R⁴ may also represent C₁₋₆alkyl substituted with cyano or amino carbonyl;

R⁵ is hydrogen or C₁₋₄alkyl;

L is -X¹-R⁶ or -X²-Alk-R⁷ wherein

R⁶ and R⁷ each independently are phenyl or phenyl substituted with one, two, three, four or

five substituents each independently selected from halo, hydroxy, C₁₋₆alkyl, C₁₋₆alkyloxy, C₁₋₆alkylcarbonyl, C₁₋₆alkyloxycarbonyl, formyl, cyano, nitro, amino, and trifluoromethyl; or when Y is CR⁵ then R⁶ and R⁷ may also be selected from phenyl substituted with one, two, three, four or five substituents each independently selected from aminocarbonyl, trihalomethyloxy and trihalomethyl; or when Y is N then R⁶ and R⁷ may also be selected from indanyl or indolyl, each of said indanyl or indolyl may be substituted with one, two, three, four or five substituents each independently selected from halo, hydroxy, C₁₋₆alkyl, C₁₋₆alkyloxy, C₁₋₆alkylcarbonyl, C₁₋₆alkyloxycarbonyl, formyl, cyano, nitro, amino, and trifluoromethyl; X¹ and X² are each independently -NR³-, -NH-NH-, -N=N-, -O-, -S-, -S(=O)- or -S(=O)₂-; Alk is C₁₋₄alkanediyl; or when Y is CR⁵ then L may also be selected from C₁₋₁₀alkyl, C₃₋₁₀alkenyl, C₃₋₁₀alkynyl, C₃₋₇cycloalkyl, or C₁₋₁₀alkyl substituted with one or two substituents independently selected from C₃₋₇cycloalkyl, indanyl, indolyl and phenyl, wherein said phenyl, indanyl and indolyl may be substituted with one, two, three, four or where possible five substituents each independently selected from halo, hydroxy, C₁₋₆alkyl, C₁₋₆alkyloxy, cyano, aminocarbonyl, C₁₋₆alkyloxycarbonyl, formyl, nitro, amino,

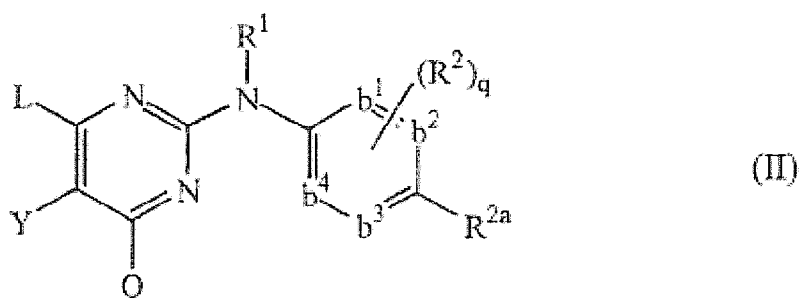
trihalomethyl, trihalomethyloxy and C₁-₆alkylcarbonyl;

aryl is phenyl or phenyl substituted with one, two, three, four or five substituents each independently selected from halo, C₁-₆alkyl, C₁-₆alkyloxy, cyano, nitro and trifluoromethyl;

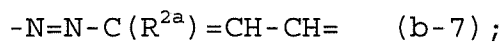
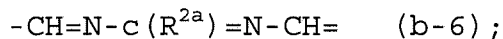
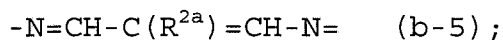
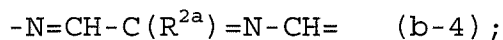
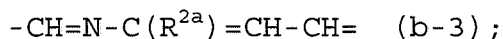
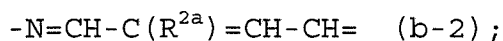
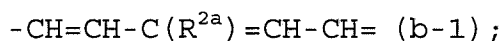
Het is an aliphatic or aromatic heterocyclic radical; said aliphatic heterocyclic radical is selected from pyrrolidinyl, piperidinyl, homopiperidinyl, piperazinyl, morpholinyl, tetrahydrofuranyl and tetrahydrothienyl

wherein each of said aliphatic heterocyclic radical may optionally be substituted with an oxo group; and said aromatic heterocyclic radical is selected from pyrrolyl, furanyl, thienyl, pyridyl, pyrimidinyl, pyrazinyl and pyridazinyl wherein each of said aromatic heterocyclic radical may optionally be substituted with hydroxy,

or a compound of formula II



the N-oxides, the pharmaceutically acceptable addition salts, quaternary amines and the stereochemically isomeric forms thereof, wherein
 $-b^1=b^2-C(R^{2a})=b^3-b^4-$ represents a bivalent radical of formula

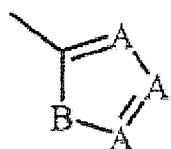


q is 0, 1, 2; or where possible q is 3 or 4;

R¹ is hydrogen, aryl, formyl, C₁₋₆alkylcarbonyl, C₁₋₆alkyl, C₁₋₆alkyloxycarbonyl, C₁₋₆alkyl substituted with formyl, C₁₋₆alkylcarbonyl, C₁₋₆alkyloxycarbonyl;

R^{2a} is cyano, aminocarbonyl, mono- or di(methyl)aminocarbonyl, C₁₋₆alkyl substituted with cyano, aminocarbonyl or mono- or di(methyl)aminocarbonyl, C₂₋₆alkenyl substituted with cyano, or C₂₋₆alkynyl substituted with cyano;

each R² independently is hydroxy, halo, C₁₋₆alkyl optionally substituted with cyano or -C(=O)R⁶, C₃₋₇cycloalkyl, C₂₋₆alkenyl optionally substituted with one or more halogen atoms or cyano, C₂₋₆alkynyl optionally substituted with one or more halogen atoms or cyano, C₁₋₆alkyloxy, C₁₋₆alkyloxycarbonyl, carboxyl, cyano, nitro, amino, mono- or di(C₁₋₆alkyl)amino, polyhalomethyl, polyhalomethyloxy, polyhalomethylthio, -S(=O)OR⁶, -NH-S(=O)_pR⁶, -C(=O)R⁶, -NHC(=O)H, -C(=O)NHNH₂, -NHC(=O)R⁶, -C(=NH)R⁶ or a radical of formula



(c)

wherein each A independently is N, CH or CR⁶;

B is NH, O, S or NR⁶;

p is 1 or 2; and

R⁶ is methyl, amino, mono- or dimethylamino or polyhalomethyl;

L is C₁₋₁₀alkyl, C₂₋₁₀alkenyl, C₂₋₁₀alkynyl, C₃₋₇cycloalkyl, whereby each of said aliphatic group may be substituted with one or two substituents independently selected from

* C₃₋₇cycloalkyl,

* indolyl or isoindolyl, each optionally substituted with one, two, three or four substituents each independently selected from halo, C₁₋₆alkyl, hydroxy, C₁₋₆alkyloxy, cyano, aminocarbonyl, nitro, amino, polyhalomethyl, polyhalomethyloxy and C₁₋₆alkylcarbonyl,

* phenyl, pyridinyl, pyrimidinyl, pyrazinyl or pyridazinyl, wherein each of said aromatic rings may optionally be substituted with one, two, three, four or five substituents each independently selected from the substituents defined in R²; or

L is -X-R³ wherein

R³ is phenyl, pyridinyl, pyrimidinyl, pyrazinyl or pyridazinyl, wherein each of said aromatic rings may optionally be substituted

with one, two, three, four or five substituents each independently selected from the substituents defined in R²; and X is -NH¹-, -NH-NH-, -N=N-, -O-, -C(=O)-, -CHOH-, -S-, -S(=O)- or -S(=O)₂-;

Q represents hydrogen, C₁₋₆alkyl, halo, polyhaloC₁₋₆alkyl or -NR⁴R⁵; and

R⁴ and R⁵ are each independently selected from hydrogen, hydroxy, C₁₋₁₂alkyl, C₁₋₁₂alkyloxy, C₁₋₁₂alkylcarbonyl, C₁₋₁₂alkyloxycarbonyl, aryl, amino, mono- or di(C₁₋₁₂alkyl)amino, mono- or di(C₁₋₁₂alkyl)aminocarbonyl wherein each of the aforementioned C₁₋₁₂alkyl groups may optionally and each individually be substituted with one or two substituents each independently selected from hydroxy, C₁₋₆alkyloxy, hydroxyc₁₋₆alkyloxy, carboxyl, C₁₋₆alkyloxycarbonyl, cyano, amino, imino, mono- or di(C₁₋₆alkyl)amino, polyhalomethyl, polyhalomethyloxy, polyhalomethylthio, -S(O)_pR⁶, -NH-S(=O)_pR⁶, -C(=O)R⁶, -NHC(=O)H, -C(=O)NHNH₂, -NHC(O)R⁶, -C(=NH)R⁶, aryl and Het; or

R⁴ and R⁵ taken together may form pyrrolidinyl, piperidinyl, morpholinyl, azido or mono- or di(C₁₋₁₂alkyl)aminoC₁₋₄-alkylidene;

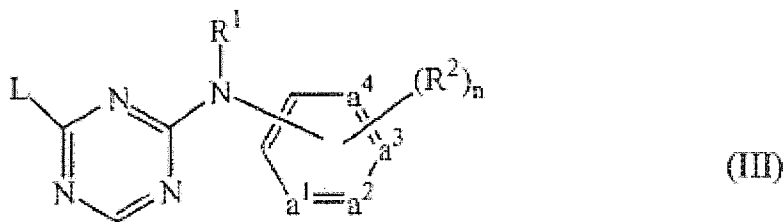
Y represents hydroxy, halo, C₃₋₇cycloalkyl, C₂₋₆alkenyl optionally substituted with one or more halogen atoms, C₂₋₆alkynyl optionally substituted with one or more halogen atoms, C₁₋₆alkyl substituted with cyano or -C(=O)R⁶, C₁₋₆alkyloxy, C₁₋₆alkyloxycarbonyl, carboxyl, cyano, nitro, amino, mono- or di(C₁₋₆alkyl)amino,

polyhalomethyl, polyhalomethyloxy,
 polyhalomethylthio, $-S(=O)_pR^6$, $-NH-S(=O)_pR^6$, $-$
 $C(=O)R^6$, $-NHC(=O)H$, $-C(=O)NHNH_2$, $-NHC(=O)R^6$, $-$
 $C(NH)R^6$ or aryl;

aryl is phenyl or phenyl substituted with one, two,
 three, four or five substituents each
 independently selected from halo, C_{1-6} alkyl, C_{3-7} cycloalkyl, C_{1-6} alkyloxy, cyano, nitro,
 polyhalo C_{1-6} alkyl and polyhalo C_{1-6} alkyloxy;

Het is an aliphatic or aromatic heterocyclic radical;
 said aliphatic heterocyclic radical is selected
 from pyrrolidinyl, piperidinyl, homopiperidinyl,
 piperazinyl, morpholinyl, tetrahydrofuranyl and
 tetrahydrothienyl wherein each of said aliphatic
 heterocyclic radical may optionally be
 substituted with an oxo group; and said aromatic
 heterocyclic radical is selected from pyrrolyl,
 furanyl, thienyl, pyridinyl, pyrimidinyl,
 pyrazinyl and pyridazinyl wherein each of said
 aromatic heterocyclic radical may optionally be
 substituted with hydroxy,

or a compound of formula III



a N-oxide, a pharmaceutically acceptable addition
 salt, a quaternary amine or a stereochemically
 isomeric form thereof, wherein
 $-a^1=a^2-a^3=a^4-$ represents a bivalent radical of formula

-CH=CH-CH=CH- (a-1);

-N=CH-CH=CH- (a-2);

-N=CH-N=CH- (a-3);

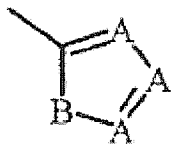
-N=CH-CH=N- (a-4);

-N=N-CH=CH- (a-5);

n is 0, 1, 2, 3 or 4; and in case $-a^1=a^2-a^3=a^4-$ is (a-1), then n may also be 5;

R^1 is hydrogen, aryl, formyl, C_{1-6} alkylcarbonyl, C_{1-6} alkyl, C_{1-6} alkyloxycarbonyl, C_{1-6} alkyl substituted with formyl, C_{1-6} alkylcarbonyl, C_{1-6} alkyloxycarbonyl; and

each R^2 independently is hydroxy, halo, C_{1-6} alkyl optionally substituted with cyano or $-C(=O)R^4$, C_{3-7} cycloalkyl, C_{2-6} alkenyl optionally substituted with one or more halogen atoms or cyano, C_{2-6} alkynyl optionally substituted with one or more halogen atoms or cyano, C_{1-6} alkyloxy, C_{1-6} alkyloxycarbonyl, carboxyl, cyano, nitro, amino, mono- or di(C_{1-6} alkyl)amino, polyhalomethyl, polyhalomethyloxy, polyhalomethylthio, $-S(=O)_pR^4$, $-NH-S(=O)_pR^4$, $-C(=O)R^4$, $-NHC(=O)R$, $-C(=O)NHNH_2$, $NHC(=O)R^4$, $-C(=NH)R^4$ or a radical of formula



(c)

wherein each A independently is N, CH or CR^4 ;

B is NH, O, S or NR^4 ;

p is 1 or 2; and

R^4 is methyl, amino, mono- or dimethylamino or polyhalomethyl;

L is C₄₋₁₀alkyl, C₂₋₁₀alkenyl, C₂₋₁₀alkynyl, C₃₋₇cycloalkyl, whereby each of said aliphatic group may be substituted with one or two substituents independently selected from

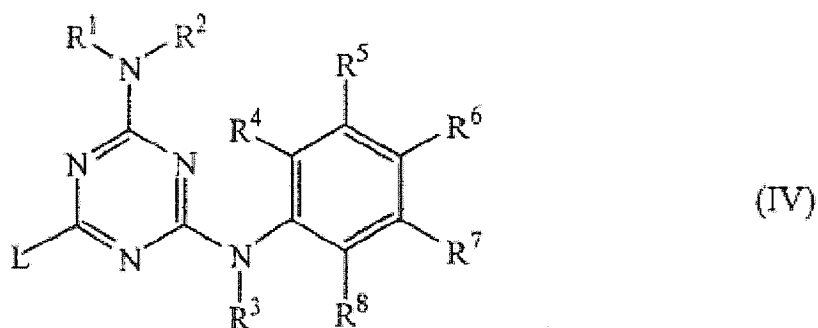
- * C₃₋₇cycloalkyl,
- * indolyl or isoindolyl, each optionally substituted with one, two, three or four substituents each independently selected from halo, C₁₋₆alkyl, hydroxy, C₁₋₆alkyloxy, cyano, aminocarbonyl, nitro, amino, polyhalomethyl, polyhalomethyloxy and C₁₋₆alkylcarbonyl,
- * phenyl, pyridinyl, pyrimidinyl, pyrazinyl or pyridazinyl, wherein each of said aromatic rings may optionally be substituted with one, two, three, four or five substituents each independently selected from the substituents defined in R²; or

L is -X-R³ wherein

R³ is phenyl, pyridinyl, pyrimidinyl, pyrazinyl or pyridazinyl, wherein each of said aromatic rings may optionally be substituted with two, three, four or five substituents each independently selected from the substituents defined in R²; and

X is -NR¹-, -NH-NH-, -N=N-, -O-, -C(=O)-, -CHOH-, -S-, -S(=O)- or -S(=O)₂-;

aryl is phenyl or phenyl substituted with one, two, three, four or five substituents each independently selected from halo, C₁₋₆alkyl, C₃₋₇cycloalkyl, C₁₋₆alkyloxy, cyano, nitro, polyhaloC₁₋₆alkyl and polyhaloC₁₋₆alkyloxy, or a compound of formula IV



the pharmaceutically acceptable acid addition salts and the stereochemically isomeric forms thereof, wherein

R^1 and R^2 are each independently selected from

hydrogen; hydroxy; amino; C_{1-6} alkyl; C_{1-6} alkyloxy; C_{1-6} alkylcarbonyl; C_{1-6} alkyloxycarbonyl; Ar^1 ; mono- or di(C_{1-6} alkyl)amino; mono- or di(C_{1-6} alkyl)aminocarbonyl; dihydro-2(3H)-furanone; C_{1-6} alkyl substituted with one or two substituents each independently selected from amino, imino, aminocarbonyl, aminocarbonylamino, hydroxy, hydroxyc C_{1-6} alkyloxy, carboxyl, mono- or di(C_{1-6} alkyl)amino, C_{1-6} alkyloxycarbonyl and thienyl; or

R^1 and R^2 taken together may form pyrrolidinyl, piperidinyl, morpholinyl, azido or mono- or di(C_{1-6} alkyl)amino C_{1-4} -alkylidene;

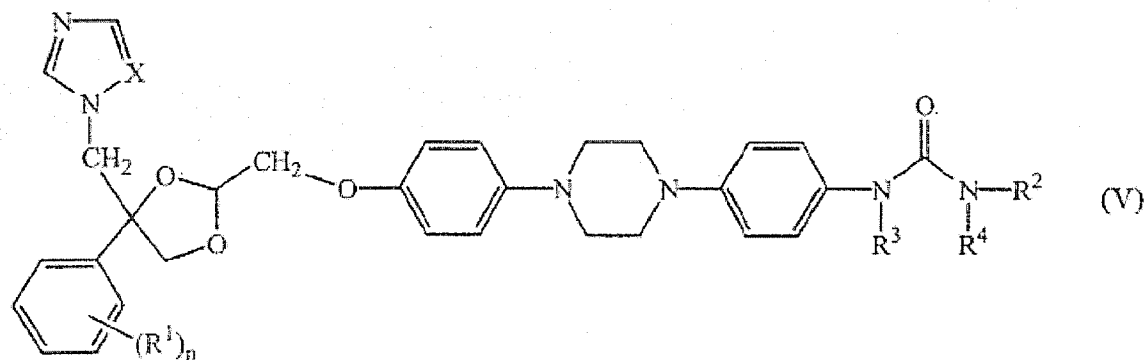
R^3 is hydrogen, Ar^1 , C_{1-6} alkylcarbonyl, C_{1-6} alkyl, C_{1-6} alkyloxycarbonyl, C_{1-6} alkyl substituted with C_{1-6} alkyloxycarbonyl; and

R^4 , R^5 , R^6 , R^7 and R^8 are each independently selected from hydrogen, hydroxy, halo, C_{1-6} alkyl, C_{1-6} alkyloxy, cyano, aminocarbonyl, nitro, amino, trihalomethyl or trihalomethyloxy;

- L is C₁₋₁₀alkyl, C₃₋₁₀alkenyl; C₃₋₁₀alkynyl; C₃₋₇cycloalkyl, or
- L is C₁₋₁₀alkyl substituted with one or two substituents independently selected from C₃₋₇cycloalkyl; indolyl or indolyl substituted with one, two, three or four substituents each independently selected from halo, C₁₋₆alkyl, C₁₋₆alkyloxy, cyano, aminocarbonyl, nitro, amino, trihalomethyl, trihalomethyloxy, C₁₋₆alkylcarbonyl; phenyl or phenyl substituted with one, two, three, four or five substituents each independently selected from halo, hydroxy, C₁₋₆alkyl, C₁₋₆alkyloxy, cyano, aminocarbonyl, nitro, amino, trihalomethyl, trihalomethyloxy, C₁₋₆alkylcarbonyl; and,
- Ar¹ is phenyl, or phenyl substituted with one, two or three substituents each independently selected from halo, C₁₋₆alkyl, C₁₋₆alkyloxy, cyano, nitro or trifluoromethyl;
- with the proviso that compounds (a) to (o)

Co. No.	Alk	R ¹ /R ²	R ³	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸
a	1-(4-(2-methylpropyl)phenyl)ethyl	H/H	H	CH ₃	H	H	H	H
b	1-(4-(2-methylpropyl)phenyl)ethyl	H/H	H	H	H	NO ₂	H	H
c	1-(4-(2-methylpropyl)phenyl)ethyl	H/H	C ₆ H ₅	H	H	H	H	H
d	1-(4-(2-methylpropyl)phenyl)ethyl	H/H	H	NO ₂	H	CH ₃	H	H
e	1-(4-(2-methylpropyl)phenyl)ethyl	H/H	H	H	H	NH ₂	H	H
f	4-(2-methylpropyl)phenylmethyl	H/H	H	H	CF ₃	H	H	H
g	1-(4-(2-methylpropyl)phenyl)ethyl	H/H	H	H	H	Cl	H	H
h	4-(2-methylpropyl)phenylmethyl	H/H	H	H	H	H	H	H
i	3,4-dimethoxyphenylmethyl	H/H	H	H	H	H	H	H
j	2,3-dimethoxyphenylmethyl	H/H	H	H	H	H	H	H
k	3,4-diethoxyphenylmethyl	H/H	H	H	H	H	H	H
l	2-(3,5-(1,1-dimethylethyl)-4-hydroxy-phenyl)ethyl	H/H	H	H	H	H	H	H
m	2-(3,5-(1,1-dimethylethyl)-4-hydroxy-phenyl)ethyl	H/H	H	H	t-Bu	OH	t-Bu	H
n	Phenylmethyl	H/H	H	CH ₃	H	H	H	H
o	Phenylmethyl	H/H	H	H	H	H	H	H

are not included,
or a compound of formula V



the N-oxide forms, the pharmaceutically acceptable
acid addition salts and stereochemically isomeric
forms thereof,

wherein

n is zero, 1, 2 or 3;

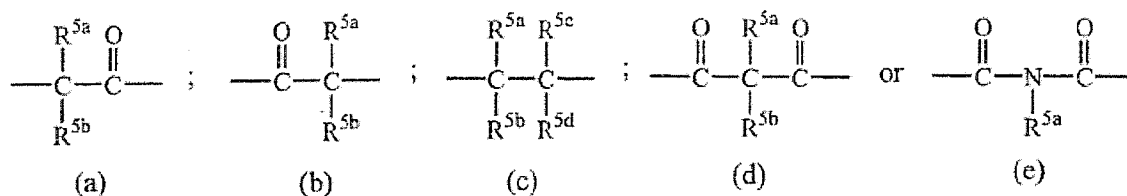
X is N or CH;

each R^1 independently is halo, nitro, cyano, amino, hydroxy, C_{1-4} alkyl, C_{1-4} alkyloxy or trifluoromethyl;

R^2 is hydrogen; C_{3-7} alkenyl; C_{3-7} alkynyl, aryl; C_{3-7} cycloalkyl; C_{1-6} alkyl or C_{1-6} alkyl substituted with hydroxy, C_{1-4} alkyloxy, C_{3-7} cycloalkyl or aryl;

R^3 and R^4 each independently are hydrogen, C_{1-6} alkyl, C_{3-7} cycloalkyl or aryl; or

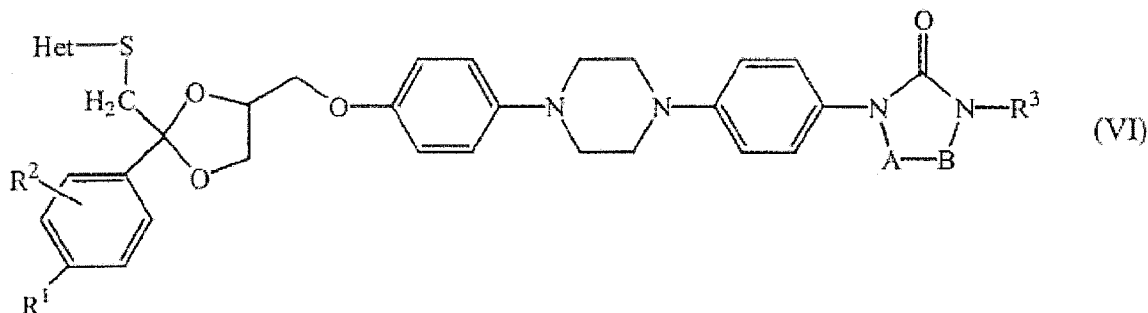
R^3 and R^4 taken together form a bivalent radical $-R^3-R^4-$ of formula:



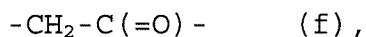
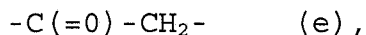
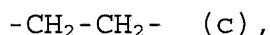
wherein R^{5a} , R^{5b} , R^{5c} , R^{5d} each independently are hydrogen, C_{1-6} alkyl or aryl; and

aryl is phenyl or phenyl substituted with one, two or three substituents selected from halo, nitro, cyano, amino, hydroxy, C_{1-4} alkyl, C_{1-4} alkyloxy or trifluoromethyl,

or a compound of formula VI



the N-oxides, the stereochemically isomeric forms thereof, and the pharmaceutically acceptable acid addition salts, wherein A and B taken together form a bivalent radical of formula:



in the bivalent radicals- of formula (a) and (h) the hydrogen atom may be replaced by C₁₋₆alkyl; in the bivalent radicals of formula (c), (d), (e), (f), one or two hydrogen atoms may be replaced by C₁₋₆alkyl;

R¹ is hydrogen, C₁₋₆alkyl or halo;

R² is hydrogen or halo;

R³ is hydrogen; C₁₋₈alkyl; C₃₋₆cycloalkyl; or C₁₋₈alkyl substituted with hydroxy, oxo, C₃₋₆cycloalkyl or aryl;

Het is a heterocycle selected from the group consisting of pyridine; pyridine substituted with one or two substituents selected from C₁₋₆alkyl, hydroxy, C₁₋₆alkyloxy, trihalomethyl, amino, mono- or di(C₁₋₆alkyl)amino or aryl; pyrimidine; pyrimidine substituted with one or two substituents selected from C₁₋₆alkyl, hydroxy, C₁₋₆alkyloxy, trihalomethyl, amino, mono- or di(C₁₋₆alkyl)-amino or aryl; tetrazole; tetrazole substituted with C₁₋₆alkyl or aryl; triazole; triazole substituted with one or two substituents selected from C₁₋₆alkyl, hydroxy, C₁₋

₆alkyloxy, trihalomethyl, amino, mono- or di(C₁₋₆alkyl)-amino;
thiadiazole; thiadiazole substituted with one or two substituents selected from C₁₋₆alkyl, hydroxy, C₁₋₆alkyloxy, trihalomethyl, amino, mono- or di(C₁₋₆alkyl)-amino;
oxadiazole substituted with one or two substituents selected from C₁₋₆alkyl, hydroxy, C₁₋₆alkyloxy, trihalomethyl, amino, mono- or di(C₁₋₆alkyl)amino;
imidazole; imidazole substituted with one or two substituents selected from C₁₋₆alkyl, hydroxy, C₁₋₆alkyloxy, trihalomethyl, amino, mono- or di(C₁₋₆alkyl)amino;
thiazole; thiazole substituted with one or two substituents selected from C₁₋₆alkyl, hydroxy, C₁₋₆alkyloxy, trihalomethyl, amino, mono- or di(C₁₋₆alkyl)amino;
oxazole; oxazole substituted with one or two substituents selected from C₁₋₆alkyl, hydroxy, C₁₋₆alkyloxy, trihalomethyl, amino, mono- or di(C₁₋₆alkyl)amino;
aryl is phenyl or phenyl substituted with C₁₋₆alkyl or halo, and the heterocyclic radical "Het" is bound to the sulfur atom via a carbon atom.

2. (previously presented) Particles according to claim 1, wherein the copolymer of N-vinylpyrrolidone is a copolymer with vinyl acetate.
3. (canceled)

4. (previously presented) Particles according to claim 1, which comprise a surfactant and wherein the surfactant is a PEG-n-hydrogenated castor oil, or a low molecular weight polyoxyethylene polyoxypropylene block copolymer.
5. (canceled)
6. (currently amended) Particles according to claim 1, further comprising citric acid in amounts of up to 5% b.w. by weight of the total weight of the rate-controlled release particles.
7. (canceled)
8. (currently amended) Particles according to ~~claim 7~~ claim 1, wherein the homo- or copolymer of N-vinylpyrrolidone is used in amounts of from 50 to 65 % b.w. by weight of the total weight of the rate-controlled release particles.
9. (canceled)
10. (previously presented) Particles according to claim 1, wherein the controlled release is a sustained release.
11. (currently amended) Particles according to claim 10, comprising the hydroxypropyl methyl cellulose in

amounts of from 5 to 10 % ~~b.w.~~ by weight of the total weight of the rate-controlled release particles.

12. (canceled)
13. (previously presented) Particles according to claim 1, comprising a compound selected from the group consisting of
- 4-[[4-[(2,4,6-trimethylphenyl)amino]-2-pyrimidyl]amino]benzonitrile;
- 4-[[2-[(cyanophenyl)amino]-4-pyrimidinyl]amino]-3,5-dimethylbenzonitrile;
- 4-[[4-amino-5-chloro-6-[(2,4,6-trimethylphenyl)amino]-2-pyrimidinyl]-amino]benzonitrile;
- 4-[[5-chloro-4-[(2,4,6-trimethylphenyl)amino]-2-pyrimidinyl]amino]benzonitrile;
- 4-[[5-bromo-4-(4-cyano-2,6-dimethylphenoxy)-2-pyrimidin]amino]benzonitrile;
- 4-[[4-amino-5-chloro-6-[(4-cyano-2,6-dimethylphenyl)amino]-2-pyrimidinyl]amino]benzonitrile;
- 4-[[5-bromo-6-[(4-cyano-2,6-dimethylphenyl)amino]-2-pyrimidinyl]-amino]benzonitrile;
- 4-[[4-amino-5-chloro-6-[(4-cyano-2,6-dimethylphenoxy)-2-pyrimidinyl]amino]benzonitrile;

4-[[4-amino-5-bromo-6-(4-cyano-2,6-dimethylphenoxy)-2-pyrimidinyl]amino]benzonitrile;
4-[[4-[(2,4,6-trimethylphenyl)amino]-1,3,5-triazin-2-yl]-amino]benzonitrile;
4-[[4-amino-6-[(2,6-dichlorophenyl)methyl]-1,3,5-triazin-2-yl]-amino]benzonitrile;
4-[[4-[(2,6-dichlorophenyl)methyl]-6-(hydroxyamino)-1,3,5-triazin-2-yl]amino]benzonitrile;
1[4-[4-[4-[4-(2,4-difluorophenyl)-4-(1H-1,2,4-triazol-1-yl)methyl]-1,3-dioxolan-2-yl]methoxy]phenyl)-1-piperazinyl]-phenyl]-3-(1-methylethyl)-2-imidazolidinone;
(-)-[2S-[2alpha, 4alpha(S*)]]-4-[4-[4-[4-[2-(4-chlorophenyl)-2-[[4-methyl-4H-1,2,4-triazol-3-yl]thio]methyl]-1,3-dioxolan-4-yl]methoxyl]phenyl]-1-piperazinyl]phenyl]-2,4-dihydro-2-(1-methyl-propyl)-3H-1,2,4-triazol-3-one,
a N-oxide, a pharmaceutically acceptable addition salt or a stereochemically isomeric form thereof.

14. (previously presented) Pharmaceutical dosage form, comprising particles according to a claim 1.
15. (previously presented) Pharmaceutical dosage forms according to claim 14, further comprising one or more pharmaceutically acceptable excipients.

16. (currently amended) Particles according to claim 4, which meet one or both of the following requirements:
- the surfactant has a HLB-value of from 10 to 18;
 - the surfactant is present in the particles in an amount of from 5 to 20% by weight of the total weight of the rate-controlled release particles.
17. to 19. (canceled)
20. (currently amended) Particles according to claim 1, consisting essentially of the active ingredient, from 40 to 70% by weight of the total weight of the rate-controlled release particles of the a homo- or copolymer of N-vinylpyrrolidone, from 5 to 20% by weight of the total weight of the rate-controlled release particles of the surfactant, up to 5% by weight of the total weight of the rate-controlled release particles of citric acid, and from 5 to 25% by weight of the total weight of the rate-controlled release particles of hydroxypropyl methyl cellulose.
21. (previously presented) Particles according to claim 20, wherein the surfactant has a HLB-value of from 10 to 18.
22. (previously presented) Particles according to claim 21, wherein the surfactant is a PEG-n-hydrogenated

castor oil and/or a low molecular weight
polyoxyethylene polyoxypropylene block copolymer.

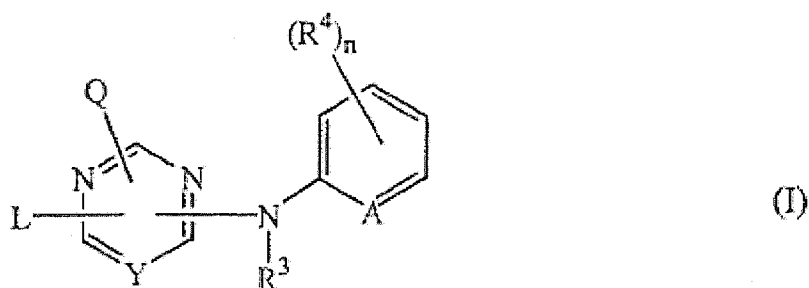
23. (canceled)

24. (canceled)

25. (canceled)

26. (currently amended) ~~Particles according to claim 1~~
Rate-controlled release particles, comprising, in a
polymer matrix consisting of from 40 to 70% by weight
of the total weight of the rate-controlled release
particles of a homo- or copolymer of N-
vinylpyrrolidone, an active ingredient as a solid
dispersion in the polymeric matrix and from 5 to 25%
by weight of the total weight of the rate-controlled
release particles of hydroxypropyl methyl cellulose,
and optionally further comprising a surfactant,
wherein the rate-controlled release particles are
obtained by forming a homogeneous mixture of the
components in the form of a melt, extruding said
mixture and shaping of the extrudate, wherein the
homo- or copolymer of N-vinylpyrrolidone has a
Fikentscher K value of from 17 to 90, and wherein the
active ingredient is

a compound of formula I



a N-oxide, a pharmaceutically acceptable addition salt or a stereochemically isomeric form thereof, wherein

Y is CR⁵ or N;

A is CH, CR⁴ or N;

n is 0, 1, 2, 3 or 4;

Q is -NR¹R² or when Y is CR⁵ then Q may also be hydrogen;

R¹ and R² are each independently selected from hydrogen, hydroxy, C₁₋₁₂alkyl, C₁₋₁₂alkyloxy, C₁₋₁₂alkylcarbonyl, C₁₋₁₂alkyloxycarbonyl, aryl, amino, mono- or di(C₁₋₁₂alkyl)amino, mono- or di(C₁₋₁₂alkyl)aminocarbonyl

wherein each of the aforementioned C₁₋₁₂alkyl groups may optionally and each individually be substituted with one or two substituents each independently selected from hydroxy, C₁₋₆alkyloxy, hydroxy-C₁₋₆alkyloxy, carboxyl, C₁₋₆alkyloxycarbonyl, cyano, amino, imido, aminocarbonyl, aminocarbonylamino, mono- or di(C₁₋₆alkyl)amino, aryl and Het; or

R¹ and R² taken together may form pyrrolidinyl, piperidinyl, morpholinyl, azido or mono- or di(C₁₋₁₂alkyl)aminoC₁₋₄-alkylidene;

R³ is hydrogen, aryl, C₁₋₆alkylcarbonyl, C₁₋₆alkyl, C₁₋₆alkyloxycarbonyl, C₁₋₆alkyl substituted with C₁₋₆alkyloxycarbonyl; and

each R⁴ independently is hydroxy, halo, C₁₋₆alkyl, C₁₋₆alkyloxy, cyano, aminocarbonyl, nitro, amino, trihalomethyl, trihalomethyloxy, or when Y is CR⁵ then R⁴ may also represent C₁₋₆alkyl substituted with cyano or amino carbonyl;

R⁵ is hydrogen or C₁₋₄alkyl;

L is -X¹-R⁶ or -X²-Alk-R⁷ wherein

R⁶ and R⁷ each independently are phenyl or phenyl substituted with one, two, three, four or five substituents each independently selected from halo, hydroxy, C₁₋₆alkyl, C₁₋₆alkyloxy, C₁₋₆alkylcarbonyl, C₁₋₆alkyloxycarbonyl, formyl, cyano, nitro, amino, and trifluoromethyl; or when Y is CR⁵ then R⁶ and R⁷ may also be selected from phenyl substituted with one, two, three, four or five substituents each independently selected from aminocarbonyl, trihalomethyloxy and trihalomethyl; or when Y is N then R⁶ and R⁷ may also be selected from indanyl or indolyl, each of said indanyl or indolyl may be substituted with one, two, three, four or five substituents each independently selected from halo, hydroxy, C₁₋₆alkyl, C₁₋₆alkyloxy, C₁₋₆alkylcarbonyl, C₁₋₆alkyloxycarbonyl, formyl, cyano, nitro, amino, and trifluoromethyl;

X¹ and X² are each independently -NR³-, -NH-NH-, -N=N-, -O-, -S-, -S(=O)- or -S(=O)₂-;

Alk is C₁₋₄alkanediyl; or

when Y is CR⁵ then L may also be selected from C₁₋₁₀alkyl, C₃₋₁₀alkenyl, C₃₋₁₀alkynyl, C₃₋₇cycloalkyl,

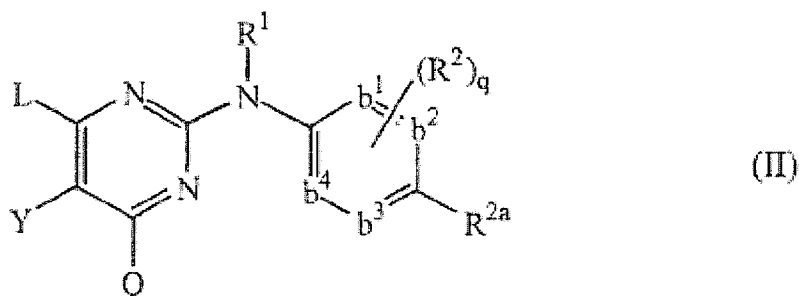
or C₁₋₁₀alkyl substituted with one or two
substituents independently selected from C₃₋
₇cycloalkyl, indanyl, indolyl and phenyl, wherein
said phenyl, indanyl and indolyl may be
substituted with one, two, three, four or where
possible five substituents each independently
selected from halo, hydroxy, C₁₋₆alkyl, C₁₋
₆alkyloxy, cyano, aminocarbonyl, C₁₋
₆alkyloxycarbonyl, formyl, nitro, amino,
trihalomethyl, trihalomethyloxy and C₁₋
₆alkylcarbonyl;

aryl is phenyl or phenyl substituted with one, two,
three, four or five substituents each
independently selected from halo, C₁₋₆alkyl, C₁₋
₆alkyloxy, cyano, nitro and trifluoromethyl;

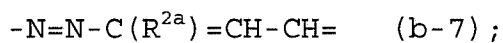
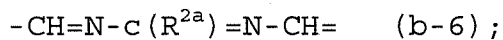
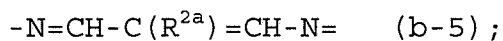
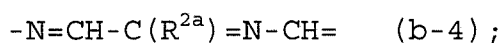
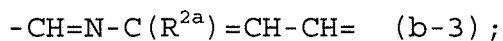
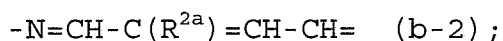
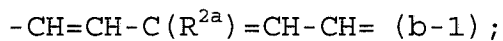
Het is an aliphatic or aromatic heterocyclic radical;
said aliphatic heterocyclic radical is selected
from pyrrolidinyl, piperidinyl, homopiperidinyl,
piperazinyl, morpholinyl, tetrahydrofuranyl and
tetrahydrothienyl

wherein each of said aliphatic heterocyclic radical
may optionally be substituted with an oxo group;
and said aromatic heterocyclic radical is
selected from pyrrolyl, furanyl, thienyl,
pyridyl, pyrimidinyl, pyrazinyl and pyridazinyl
wherein each of said aromatic heterocyclic
radical may optionally be substituted with
hydroxy,

or a compound of formula II



the N-oxides, the pharmaceutically acceptable addition salts, quaternary amines and the stereochemically isomeric forms thereof, wherein
-b¹=b²-C(R^{2a})=b³-b⁴= represents a bivalent radical of formula

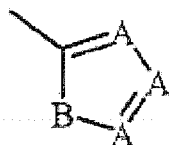


q is 0, 1, 2; or where possible q is 3 or 4;

R¹ is hydrogen, aryl, formyl, C₁₋₆alkylcarbonyl, C₁₋₆alkyl, C₁₋₆alkyloxycarbonyl, C₁₋₆alkyl substituted with formyl, C₁₋₆alkylcarbonyl, C₁₋₆alkyloxycarbonyl;

R^{2a} is cyano, aminocarbonyl, mono- or di(methyl)aminocarbonyl, C₁₋₆alkyl substituted with cyano, aminocarbonyl or mono- or di(methyl)aminocarbonyl, C₂₋₆alkenyl substituted with cyano, or C₂₋₆alkynyl substituted with cyano;
each R² independently is hydroxy, halo, C₁₋₆alkyl optionally substituted with cyano or -C(=O)R⁶, C₃₋₇cycloalkyl, C₂₋₆alkenyl optionally substituted with one or more halogen atoms or cyano, C₂₋

alkynyl optionally substituted with one or more
halogen atoms or cyano, C₁₋₆alkyloxy, C₁₋
alkyloxycarbonyl, carboxyl, cyano, nitro, amino,
mono- or di(C₁₋₆alkyl)amino, polyhalomethyl,
polyhalomethyloxy, polyhalomethylthio, -S(=O)OR⁶,
-NH-S(=O)_pR⁶, -C(=O)R⁶, -NHC(=O)H, -C(=O)NHNH₂, -
NHC(=O)R⁶, -C(=NH)R⁶ or a radical of formula



(c)

wherein each A independently is N, CH or CR⁶;

B is NH, O, S or NR⁶;

p is 1 or 2; and

R⁶ is methyl, amino, mono- or dimethylamino or
polyhalomethyl;

L is C₁₋₁₀alkyl, C₂₋₁₀alkenyl, C₂₋₁₀alkynyl, C₃₋
7cycloalkyl, whereby each of said aliphatic group
may be substituted with one or two substituents
independently selected from

* C₃₋₇cycloalkyl,

* indolyl or isoindolyl, each optionally
substituted with one, two, three or four
substituents each independently selected from
halo, C₁₋₆alkyl, hydroxy, C₁₋₆alkyloxy, cyano,
aminocarbonyl, nitro, amino, polyhalomethyl,
polyhalomethyloxy and C₁₋₆alkylcarbonyl,

* phenyl, pyridinyl, pyrimidinyl, pyrazinyl or
pyridazinyl, wherein each of said aromatic
rings may optionally be substituted with one,

two, three, four or five substituents each independently selected from the substituents defined in R²; or

L is -X-R³ wherein

R³ is phenyl, pyridinyl, pyrimidinyl, pyrazinyl or pyridazinyl, wherein each of said aromatic rings may optionally be substituted with one, two, three, four or five substituents each independently selected from the substituents defined in R²; and

X is -NH¹-, -NH-NH-, -N=N-, -O-, -C(=O)-, -CHOH-, -S-, -S(=O)- or -S(=O)₂-;

Q represents hydrogen, C₁₋₆alkyl, halo, polyhaloC₁₋₆alkyl or -NR⁴R⁵; and

R⁴ and R⁵ are each independently selected from

hydrogen, hydroxy, C₁₋₁₂alkyl, C₁₋₁₂alkyloxy, C₁₋₁₂alkylcarbonyl, C₁₋₁₂alkyloxycarbonyl, aryl, amino, mono- or di(C₁₋₁₂alkyl)amino, mono- or di(C₁₋₁₂alkyl)aminocarbonyl wherein each of the aforementioned C₁₋₁₂alkyl groups may optionally and each individually be substituted with one or two substituents each independently selected from hydroxy, C₁₋₆alkyloxy, hydroxyc₁₋₆alkyloxy, carboxyl, C₁₋₆alkyloxycarbonyl, cyano, amino, imino, mono- or di(C₁₋₆alkyl)amino, polyhalomethyl, polyhalomethyloxy, polyhalomethylthio, -S(O)_pR⁶, -NH-S(=O)_pR⁶, -C(=O)R⁶, -NHC(=O)H, -C(=O)NHNH₂, -NHC(O)R⁶, -C(=NH)R⁶, aryl and Het; or

R⁴ and R⁵ taken together may form pyrrolidinyl,

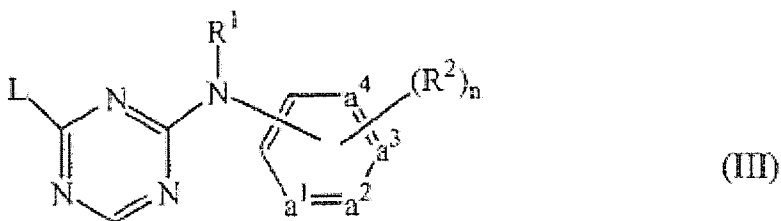
piperidinyl, morpholinyl, azido or mono- or di(C₁₋₁₂alkyl)aminoC₁₋₄-alkylidene;

Y represents hydroxy, halo, C₃₋₇cycloalkyl, C₂₋₆alkenyl optionally substituted with one or more halogen atoms, C₂₋₆alkynyl optionally substituted with one or more halogen atoms, C₁₋₆alkyl substituted with cyano or -C(=O)R⁶, C₁₋₆alkyloxy, C₁₋₆alkyloxycarbonyl, carboxyl, cyano, nitro, amino, mono- or di(C₁₋₆alkyl)amino, polyhalomethyl, polyhalomethyloxy, polyhalomethylthio, -S(=O)_pR⁶, -NH-S(=O)_pR⁶, -C(=O)R⁶, -NHC(=O)H, -C(=O)NHNH₂, -NHC(=O)R⁶, -C(NH)R⁶ or aryl;

aryl is phenyl or phenyl substituted with one, two, three, four or five substituents each independently selected from halo, C₁₋₆alkyl, C₃₋₇cycloalkyl, C₁₋₆alkyloxy, cyano, nitro, polyhaloC₁₋₆alkyl and polyhaloC₁₋₆alkyloxy;

Het is an aliphatic or aromatic heterocyclic radical; said aliphatic heterocyclic radical is selected from pyrrolidinyl, piperidinyl, homopiperidinyl, piperazinyl, morpholinyl, tetrahydrofuranyl and tetrahydrothienyl wherein each of said aliphatic heterocyclic radical may optionally be substituted with an oxo group; and said aromatic heterocyclic radical is selected from pyrrolyl, furanyl, thienyl, pyridinyl, pyrimidinyl, pyrazinyl and pyridazinyl wherein each of said aromatic heterocyclic radical may optionally be substituted with hydroxy,

or a compound of formula III



a N-oxide, a pharmaceutically acceptable addition salt, a quaternary amine or a stereochemically isomeric form thereof, wherein

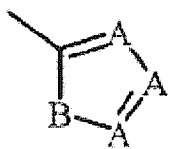
-a¹=a²-a³=a⁴- represents a bivalent radical of formula

$$-\text{CH}=\text{CH}-\text{CH}=\text{CH}- \quad (\text{a}-1) ;$$
$$-\text{N}=\text{CH}-\text{CH}=\text{CH}- \quad (\text{a-2}) ;$$
$$-\text{N}=\text{CH}-\text{N}=\text{CH}- \quad (\text{a-3}) ;$$
$$-\text{N}=\text{CH}-\text{CH}=\text{N}- \quad (\text{a-4}) ;$$
$$-\text{N}=\text{N}-\text{CH}=\text{CH}- \quad (\text{a-5}) ;$$

n is 0, 1, 2, 3 or 4; and in case $-a^1=a^2-a^3=a^4-$ is $(a-1)$, then n may also be 5;

R¹ is hydrogen, aryl, formyl, C₁₋₆alkylcarbonyl, C₁₋₆alkyl, C₁₋₆alkyloxycarbonyl, C₁₋₆alkyl substituted with formyl, C₁₋₆alkylcarbonyl, C₁₋₆alkyloxycarbonyl; and

each R² independently is hydroxy, halo, C₁₋₆alkyl optionally substituted with cyano or -C(=O)R⁴, C₃₋₇cycloalkyl, C₂₋₆alkenyl optionally substituted with one or more halogen atoms or cyano, C₂₋₆alkynyl optionally substituted with one or more halogen atoms or cyano, C₁₋₆alkyloxy, C₁₋₆alkyloxycarbonyl, carboxyl, cyano, nitro, amino, mono- or di(C₁₋₆alkyl)amino, polyhalomethyl, polyhalomethyloxy, polyhalomethylthio, -S(=O)_pR⁴, -NH-S(=O)_pR⁴, -C(=O)R⁴, -NHC(=O)R, -C(=O)NHNH₂, NHC(=O)R⁴, -C(=NH)R⁴ or a radical of formula



(c)

wherein each A independently is N, CH or CR⁴;

B is NH, O, S or NR⁴;

p is 1 or 2; and

R⁴ is methyl, amino, mono- or dimethylamino or polyhalomethyl;

L is C₄₋₁₀alkyl, C₂₋₁₀alkenyl, C₂₋₁₀alkynyl, C₃₋₇cycloalkyl, whereby each of said aliphatic group may be substituted with one or two substituents independently selected from

* C₃₋₇cycloalkyl,

* indolyl or isoindolyl, each optionally substituted with one, two, three or four substituents each independently selected from halo, C₁₋₆alkyl, hydroxy, C₁₋₆alkyloxy, cyano, aminocarbonyl, nitro, amino, polyhalomethyl, polyhalomethyloxy and C₁₋₆alkylcarbonyl,

* phenyl, pyridinyl, pyrimidinyl, pyrazinyl or pyridazinyl, wherein each of said aromatic rings may optionally be substituted with one, two, three, four or five substituents each independently selected from the substituents defined in R²; or

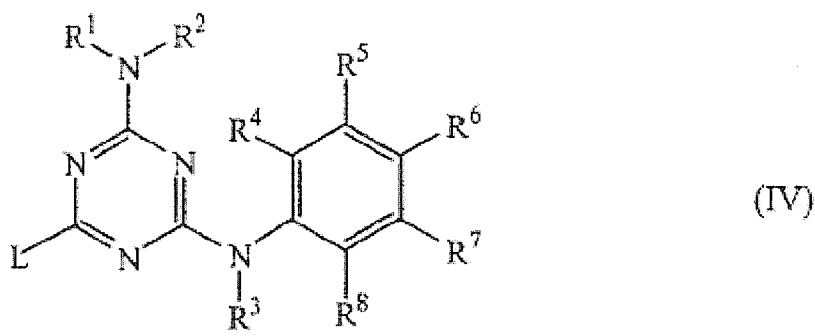
L is -X-R³ wherein

R³ is phenyl, pyridinyl, pyrimidinyl, pyrazinyl or pyridazinyl, wherein each of said aromatic rings may optionally be substituted with two, three, four or five substituents

each independently selected from the
substituents defined in R²; and

X is -NR¹-, -NH-NH-, -N=N-, -O-, -C(=O)-, -
CHOH-, -S-, -S(=O)- or -S(=O)₂-;

aryl is phenyl or phenyl substituted with one, two,
three, four or five substituents each
independently selected from halo, C₁₋₆alkyl, C₃₋
cycloalkyl, C₁₋₆alkyloxy, cyano, nitro,
polyhaloC₁₋₆alkyl and polyhaloC₁₋₆alkyloxy,
or a compound of formula IV



the pharmaceutically acceptable acid addition salts
and the stereochemically isomeric forms thereof,
wherein

R¹ and R² are each independently selected from
hydrogen; hydroxy; amino; C₁₋₆alkyl; C₁₋₆alkyloxy;
C₁₋₆alkylcarbonyl; C₁₋₆alkyloxycarbonyl; Ar¹; mono-
or di(C₁₋₆alkyl)amino; mono- or di(C₁₋
₆alkyl)aminocarbonyl; dihydro-2(3H)-furanone; C₁₋
₆alkyl substituted with one or two substituents
each independently selected from amino, imino,
aminocarbonyl, aminocarbonylamino, hydroxy,
hydroxyc₁₋₆alkyloxy, carboxyl, mono- or di(C₁₋
₆alkyl)amino, C₁₋₆alkyloxycarbonyl and thienyl; or

R¹ and R² taken together may form pyrrolidinyl, piperidinyl, morpholinyl, azido or mono- or di(C₁₋₆alkyl)aminoC₁₋₄-alkylidene;

R³ is hydrogen, Ar¹, C₁₋₆alkylcarbonyl, C₁₋₆alkyl, C₁₋₆alkyloxy, C₁₋₆alkyloxy, C₁₋₆alkyl substituted with C₁₋₆alkyloxy, C₁₋₆alkyl substituted with C₁₋₆alkyloxy; and

R⁴, R⁵, R⁶, R⁷ and R⁸ are each independently selected from hydrogen, hydroxy, halo, C₁₋₆alkyl, C₁₋₆alkyloxy, cyano, aminocarbonyl, nitro, amino, trihalomethyl or trihalomethoxy;

L is C₁₋₁₀alkyl, C₃₋₁₀alkenyl; C₃₋₁₀alkynyl; C₃₋₇cycloalkyl, or

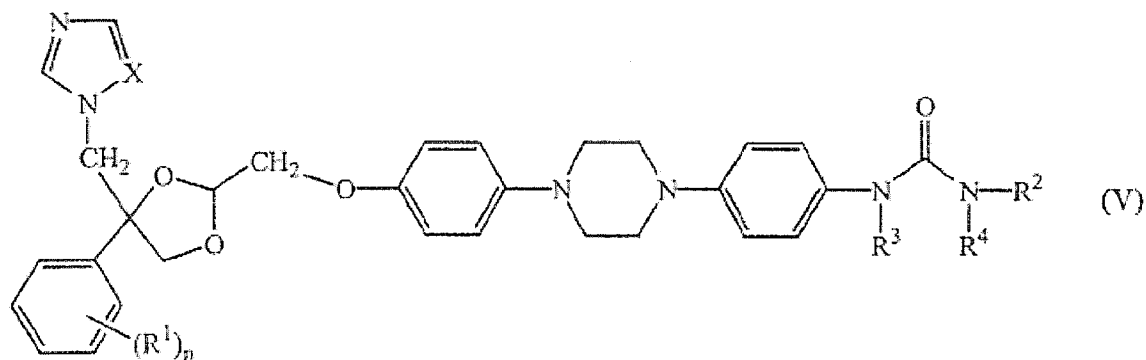
L is C₁₋₁₀alkyl substituted with one or two substituents independently selected from C₃₋₇cycloalkyl; indolyl or indolyl substituted with one, two, three or four substituents each independently selected from halo, C₁₋₆alkyl, C₁₋₆alkyloxy, cyano, aminocarbonyl, nitro, amino, trihalomethyl, trihalomethoxy, C₁₋₆alkylcarbonyl; phenyl or phenyl substituted with one, two, three, four or five substituents each independently selected from halo, hydroxy, C₁₋₆alkyl, C₁₋₆alkyloxy, cyano, aminocarbonyl, nitro, amino, trihalomethyl, trihalomethoxy, C₁₋₆alkylcarbonyl; and,

Ar¹ is phenyl, or phenyl substituted with one, two or three substituents each independently selected from halo, C₁₋₆alkyl, C₁₋₆alkyloxy, cyano, nitro or trifluoromethyl;

with the proviso that compounds (a) to (o)

Co. No.	Alk	R ¹ /R ²	R ³	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸
a	1-(4-(2-methylpropyl)phenyl)ethyl	H/H	H	CH ₃	H	H	H	H
b	1-(4-(2-methylpropyl)phenyl)ethyl	H/H	H	H	H	NO ₂	H	H
c	1-(4-(2-methylpropyl)phenyl)ethyl	H/H	C ₆ H ₅	H	H	H	H	H
d	1-(4-(2-methylpropyl)phenyl)ethyl	H/H	H	NO ₂	H	CH ₃	H	H
e	1-(4-(2-methylpropyl)phenyl)ethyl	H/H	H	H	H	NH ₂	H	H
f	4-(2-methylpropyl)phenylmethyl	H/H	H	H	CF ₃	H	H	H
g	1-(4-(2-methylpropyl)phenyl)ethyl	H/H	H	H	H	Cl	H	H
h	4-(2-methylpropyl)phenylmethyl	H/H	H	H	H	H	H	H
i	3,4-dimethoxyphenylmethyl	H/H	H	H	H	H	H	H
j	2,3-dimethoxyphenylmethyl	H/H	H	H	H	H	H	H
k	3,4-dioxyphenylmethyl	H/H	H	H	H	H	H	H
l	2-(3,5-(1,1-dimethylethyl)-4-hydroxy-phenyl)ethyl	H/H	H	H	H	H	H	H
m	2-(3,5-(1,1-dimethylethyl)-4-hydroxy-phenyl)ethyl	H/H	H	H	t-Bu	OH	t-Bu	H
n	Phenylmethyl	H/H	H	CH ₃	H	H	H	H
o	Phenylmethyl	H/H	H	H	H	H	H	H

are not included,
or a compound of formula V



the N-oxide forms, the pharmaceutically acceptable
acid addition salts and stereochemically isomeric
forms thereof,

wherein

n is zero, 1, 2 or 3;

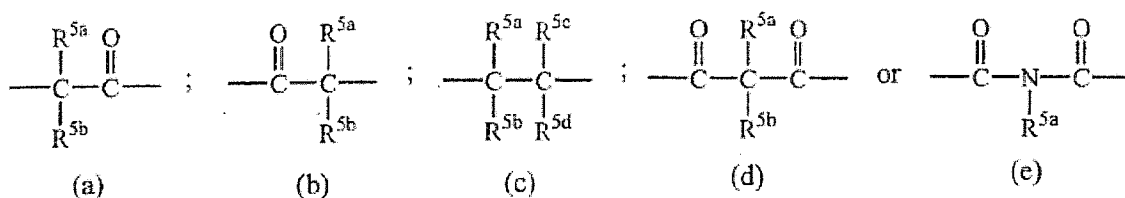
X is N or CH;

each R^1 independently is halo, nitro, cyano, amino, hydroxy, C_{1-4} alkyl, C_{1-4} alkyloxy or trifluoromethyl;

R^2 is hydrogen; C_{3-7} alkenyl; C_{3-7} alkynyl, aryl; C_{3-7} cycloalkyl; C_{1-6} alkyl or C_{1-6} alkyl substituted with hydroxy, C_{1-4} alkyloxy, C_{3-7} cycloalkyl or aryl;

R^3 and R^4 each independently are hydrogen, C_{1-6} alkyl, C_{3-7} cycloalkyl or aryl; or

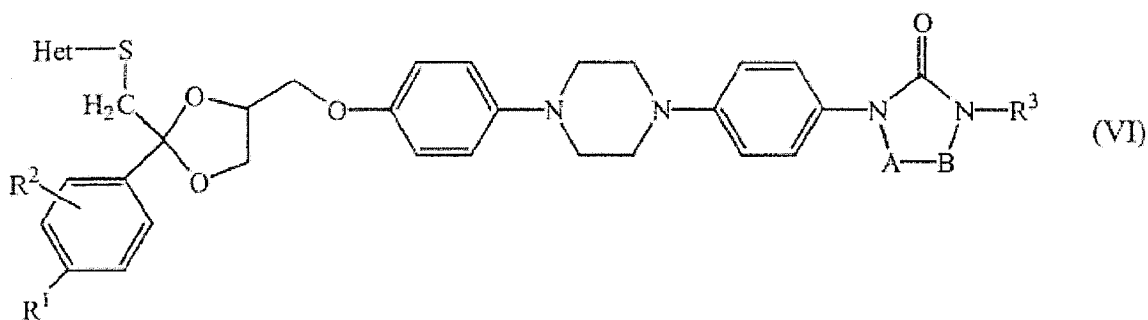
R^3 and R^4 taken together form a bivalent radical $-R^3-R^4-$ of formula:



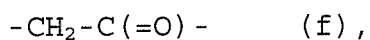
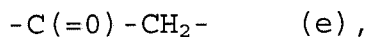
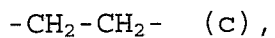
wherein R^{5a} , R^{5b} , R^{5c} , R^{5d} each independently are hydrogen, C_{1-6} alkyl or aryl; and

aryl is phenyl or phenyl substituted with one, two or three substituents selected from halo, nitro, cyano, amino, hydroxy, C_{1-4} alkyl, C_{1-4} alkyloxy or trifluoromethyl,

or a compound of formula VI



the N-oxides, the stereochemically isomeric forms thereof, and the pharmaceutically acceptable acid addition salts, wherein A and B taken together form a bivalent radical of formula:



in the bivalent radicals- of formula (a) and (h) the hydrogen atom may be replaced by C₁₋₆alkyl; in the bivalent radicals of formula (c), (d), (e), (f), one or two hydrogen atoms may be replaced by C₁₋₆alkyl;

R¹ is hydrogen, C₁₋₆alkyl or halo;

R² is hydrogen or halo;

R³ is hydrogen; C₁₋₈alkyl; C₃₋₆cycloalkyl; or C₁₋₈alkyl substituted with hydroxy, oxo, C₃₋₆cycloalkyl or aryl;

Het is a heterocycle selected from the group consisting of pyridine; pyridine substituted with one or two substituents selected from C₁₋₆alkyl, hydroxy, C₁₋₆alkyloxy, trihalomethyl, amino, mono- or di(C₁₋₆alkyl)amino or aryl; pyrimidine; pyrimidine substituted with one or two substituents selected from C₁₋₆alkyl, hydroxy, C₁₋₆alkyloxy, trihalomethyl, amino, mono- or di(C₁₋₆alkyl)-amino or aryl; tetrazole; tetrazole substituted with C₁₋₆alkyl or aryl; triazole; triazole substituted with one or two substituents selected from C₁₋₆alkyl, hydroxy, C₁₋

C_{1-6} alkyloxy, trihalomethyl, amino, mono- or di(C_{1-6} alkyl)-amino;
thiadiazole; thiadiazole substituted with one or
two substituents selected from C_{1-6} alkyl, hydroxy,
 C_{1-6} alkyloxy, trihalomethyl, amino, mono- or di(C_{1-6}
alkyl)-amino;
oxadiazole substituted with one or two
substituents selected from C_{1-6} alkyl, hydroxy, C_{1-6}
alkyloxy, trihalomethyl, amino, mono- or di(C_{1-6}
alkyl)amino;
imidazole; imidazole substituted with one or two
substituents selected from C_{1-6} alkyl, hydroxy, C_{1-6}
alkyloxy, trihalomethyl, amino, mono- or di(C_{1-6}
alkyl)amino;
thiazole; thiazole substituted with one or two
substituents selected from C_{1-6} alkyl, hydroxy, C_{1-6}
alkyloxy, trihalomethyl, amino, mono- or di(C_{1-6}
alkyl)amino;
oxazole; oxazole substituted with one or two
substituents selected from C_{1-6} alkyl, hydroxy, C_{1-6}
alkyloxy, trihalomethyl, amino, mono- or di(C_{1-6}
alkyl)amino;
aryl is phenyl or phenyl substituted with C_{1-6}
alkyl or halo, and the heterocyclic radical "Het"
is bound to the sulfur atom via a carbon atom.